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Infections Are the Major Cause of Non Relapse Mortality (NRM) after T Cell Depleted (TCD) Allogeneic Hematopoietic Stem Cell Transplantation for Advanced Myelodysplastic Syndrome

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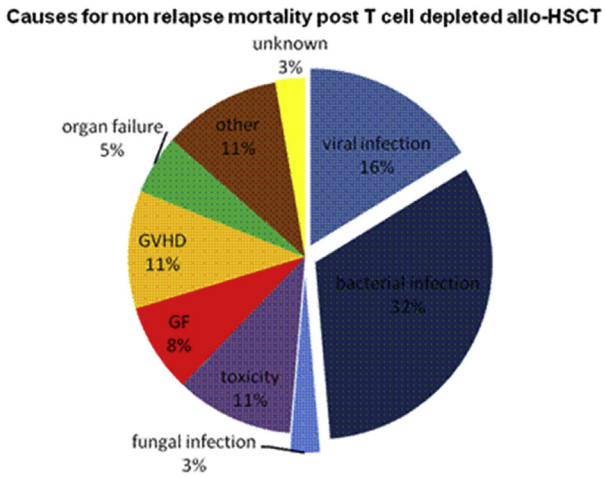
Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the only curative treatment for MDS. GVHD is one of the main causes of NRM in unmodified allo-HSCT. We aimed to study causes of NRM after TCD transplant.
108 patients with MDS underwent TCD allo-HSCT at MSKCC between 1/2001- 4/2012. Median age was 57.6 (18.1-73.0). WHO subtypes at diagnosis were: RA/RCMD 30, RAEB-I 34 & RAEB-II 44. In 73 pts disease progressed prior to transplant. 101 pts were treated before transplant (hypomethylating agents 27, induction chemotherapy 73, syngeneic transplant 1). All pts underwent conditioning with a myeloablative regimen and received ATG to prevent graft rejection (other than 4 pts). Hematopoietic stem cells source was PB in 102 pts and BM in 6 pts. BM graf**ts** were **depleted** of **T-cells** by **s**oybean aggl**u**t**i**nin followed by **s**heep RBC ro**s**e**tt**ing, and PB graft by immunomagne**t**ic CD34+ **s**elec**t**ion (I**s**olex ini**t**ially and CliniMAC**S** af**t**er 09/2011). Donors were HLA matched (79; 39 related and 40 unrelated) or mismatched (29).
The OS (with 95% confidence interval) at 1 year was 70.2% (60.5-77.9) and at 3 years 50.0 % (39.9-59.2). Cumulative incidence (CI) at 1 year of grade III-IV acute GvHD was 12.1% (6.8-19.1) and of chronic GvHD 2.8% (0.8-7.4). CI of relapse at 1 year was 11.2 % (6.1-18.0) and at 2 years 16.0% (9.7-23.6). 106 patients engrafted (2 died early and were not evaluable). The CI of NRM at 1 year was 23.3% (15.8-31.7) and at 2 years 31.8 % (23.2-40.7). The causes of death were defined according to Copelan's criteria (BBMT 2007). Infections accounted for 51% of NRM; 32% bacterial, 16% viral and 3% fungal. In a univariate landmark analysis, the only factor



associated with increased NRM was a low CD4 at 3 months ($p=0.012$). For patients with CD4<100 vs ≥100 at 3 months post transplant, the 1 year NRM was 21.9% (9.5-37.5) vs 8.6% (2.1-20.8) and at 3 years 35.4% (18.9-52.3) vs 8.6% (2.1-20.8). The CI of death due to infection was significantly higher in patients with CD4<100 vs ≥100 ($p=0.019$): 15.2% (5.4-29.5) vs 2.9% (0.2-12.9) at 1 year and 21.3% (9.2-36.8) vs 2.9% (0.2-12.9) at 3 years. There was a trend for higher NRM in older patients (>50) ($p=0.094$), with estimated incidence of 34.9% vs 20.8% at two years. The following factors were not associated with an increased NRM: etiology (de-novo vs therapy related), conditioning regimen (chemotherapy vs TBI), pre-transplant therapy (hypomethylating vs induction chemotherapy), donor (MRD vs MUD vs MM donor and mixed T cell chimerism (<50% donor chimerism) on day 100 post transplant and BM chimerism at 6 months (<95% donor chimerism).
Infections were the main cause for NRM followed by GVHD. Low CD4 count at 3 months post transplant was a strong predictor for NRM and in particular for infection related mortality. TCD allo-HSCT associated with low incidence of GvHD can serve as a platform to enhance immunity against specific common infections etiologies with viral or fungal specific cytotoxic T cells.